Paper No. 21

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte DAVID McELROY,
EMIL OROZCO, and LUCILLE LACCETTI

Appeal No. 2003-0936
Application No. 09/532,806[1]

ON BRIEF

Before WINTERS, GRON, and GREEN, Administrative Patent Judges.

GRON, Administrative Patent Judge.

DECISION ON APPEAL UNDER 35 U.S.C. § 134

Introduction

This is an appeal under 35 U.S.C. § 134 of an examiner's final rejections of Claims 1, 4-54, and 85-131, all claims pending in Application 09/532,806, under 35 U.S.C. § 112, first paragraph. Claims 1, 4-54, and 85-113 stand finally rejected for noncompliance with the written description requirement of 35 U.S.C. § 112, first

[1] Application for patent filed March 21, 2000.

paragraph. Claims 1, 4-54, and 85-131 stand finally rejected for noncompliance with the enablement requirement of 35 U.S.C. § 112, first paragraph (Brief on Appeal, p. 3 (AB 3); Examiner's Answer, p. 3 (EA 3)). Claims 1, 4-20, 33, 34, 45, 46, 48, 49, 51, 52, 85, 96, and 114, reproduced below, are representative of the full scope of the subject matter claimed.

1. An isolated nucleic acid comprising a maize GRP promoter comprising at least 95 contiguous bases of SEQ ID NO:1.

4. The isolated nucleic acid of claim 1, wherein said GRP promoter comprises from about 110 to about 3536 contiguous nucleotides of the nucleic acid sequence of SEQ ID NO:1.

5. The isolated nucleic acid of claim 1, wherein said GRP promoter comprises from about 125 to about 3536 contiguous nucleotides of the nucleic acid sequence of SEQ ID NO:1.

6. The isolated nucleic acid of claim 1, wherein said GRP promoter comprises from about 250 to about 3536 contiguous nucleotides of the nucleic acid sequence of SEQ ID NO:1.

7. The isolated nucleic acid of claim 1, wherein said GRP promoter comprises from about 400 to about 3536 contiguous nucleotides of the nucleic acid sequence of SEQ ID NO:1.

8. The isolated nucleic acid of claim 1, wherein said GRP promoter comprises from about 750 to about 3536 contiguous nucleotides of the nucleic acid sequence of SEQ ID NO:1.

9. The isolated nucleic acid of claim 1, wherein said GRP promoter comprises from about 1000 to about

3536 contiguous nucleotides of the nucleic acid sequence of SEQ ID NO:1.

10. The isolated nucleic acid of claim 1, wherein said GRP promoter comprises from about 1500 to about 3536 contiguous nucleotides of the nucleic acid sequence of SEQ ID NO:1.

11. The isolated nucleic acid of claim 1, wherein said GRP promoter comprises from about 2000 to about 3536 contiguous nucleotides of the nucleic acid sequence of SEQ ID NO:1.

12. The isolated nucleic acid of claim 1, wherein said GRP promoter comprises from about 2500 to about 3536 contiguous nucleotides of the nucleic acid sequence of SEQ ID NO:1.

13. The isolated nucleic acid of claim 1, wherein said GRP promoter comprises from about 3000 to about 3536 contiguous nucleotides of the nucleic acid sequence of SEQ ID NO:1.

14. The isolated nucleic acid of claim 1, wherein said GRP promoter comprises the nucleic acid sequence of SEQ ID NO:1.

15. The isolated nucleic acid of claim 1, further comprising an enhancer.

16. The isolated nucleic acid of claim 15, wherein said enhancer comprises an intron.

17. The isolated nucleic acid of claim 15, wherein said intron is selected from the group consisting of the rice actin 1 intron and the rice actin 2 intron.

18. The isolated nucleic acid of claim 1, further comprising a terminator.

19. The isolated nucleic acid of claim 18, wherein said terminator comprises an rbcS terminator.

20. A transgenic plant stably transformed with a selected DNA comprising a maize GRP promoter comprising at least 95 contiguous bases of SEQ ID NO:1.

33. The transgenic plant of claim 20, wherein said selected DNA further comprises a selected heterologous coding region operably linked to said GRP promoter.

34. The transgenic plant of claim 33, wherein said selected heterologous coding region encodes a protein imparting insect resistance, bacterial disease resistance, fungal disease resistance, viral disease resistance, nematode disease resistance, herbicide resistance, enhanced grain composition or quality, enhanced nutrient utilization, enhanced environment or stress resistance, reduced mycotoxin contamination, male sterility, a selectable marker phenotype, a screenable marker phenotype, a negative selectable marker phenotype, or altered plant agronomic characteristics.

45. The transgenic plant of claim 20, further defined as a monocotyledonous plant.

46. The transgenic plant of claim 45, wherein said monocotyledonous plant is selected from the group consisting of wheat, maize, rye, rice, oat, barley, turfgrass, sorghum, millet and sugarcane.

48. The transgenic plant of claim 20, further defined as a dicotyledonous plant.

49. The transgenic plant of claim 48, wherein said dicotyledonous plant is selected from the group consisting of tobacco, tomato, potato, soybean, cotton, canola, alfalfa, sunflower, and cotton.[2]

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[2] We note here that the Markush grouping of dicotyledonous plants twice recites cotton. Counsel should edit all of appellants' claims for typographical errors.

51. The transgenic plant of claim 20, further defined as a fertile R_0 transgenic plant.

52. A seed of the fertile R_0 transgenic plant of claim 51, wherein said seed comprises said selected DNA.

85. A transgenic plant[3] stably transformed with a selected DNA comprising a maize GRP promoter comprising at least 95 contiguous bases of SEQ ID NO:1.

96. The transgenic plant cell of claim 85, wherein said selected DNA further comprises a selected coding region operably linked to said maize GRP promoter.

114. A method of preparing a transgenic plant comprising the steps of:

(i) obtaining a construct comprising a maize GRP promoter comprising at least 95 contiguous bases of SEQ ID NO:1;

(ii) transforming a recipient plant cell with said construct; and

(iii) regenerating said recipient plant cell to obtain a transgenic plant transformed with said construct.

According to the examiner, (1) appellants' claims are drawn to "subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention" (EA 3); and

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[3] Note that claims dependent upon Claim 85 refer to "[t]he transgenic plant cell of claim 85" (emphasis added).

(2) "the specification, while being enabling for the isolated nucleic acid that is the maize GRP promoter described in Example 1, transgenic plants and cells comprising said promoter, and method of preparing said transgenic plant, does not reasonably provide enablement for other isolated nucleic acids that are a maize GRP promoter, or transgenic plant, seeds and cells comprising other isolated nucleic acids" (EA 3). In support of the final rejections, the examiner cites Kim, Y., et al., "A 20 nucleotide upstream element is essential for the nopaline synthase (nos) promoter activity," Plant Molecular Biology, Vol. 24, pp. 105-117 (1994), and Benfey, P., et al., "The Cauliflower Mosaic Virus 35S Promoter: Combinatorial Regulation of Transcription in Plants," Science," Vol. 250, pp. 959-966 (1990).

Discussion

1. Rejection for inadequate written description

Figure 4 describes SEQ ID NO:1 by naming its 3536 contiguous nucleotides. In so doing, appellants' specification, as originally filed, prima facie described each and every isolated 95, 110, 125, 250, 400, 750, 1000, 1500, 2000, 2500, and 3000 contiguous nucleotide segment of the 3536 contiguous nucleotides of SEQ ID NO:1 comprising a functional maize GRP promoter. Nevertheless, the examiner is concerned that appellants' specification does not

identify which of all the possible at least 95 contiguous nucleotide segments of the 3536 contiguous nucleotides of SEQ ID NO:1 described are required to promote expression of the various coding regions to be linked thereto. More specifically, the examiner argues (EA 4-5):

> 35 U.S.C. § 112 requires that Appellants describe in some manner the structure of the nucleic acid sequences that would have promoter function. Showing how or why the claimed promoter sequences function, in particular showing which structural features are necessary for the function of the maize GRP promoter, is one way in which Appellants may describe the structure of subfragments of SEQ ID NO:1 that would have promoter function. Appellants might also describe the structure of subfragments of SEQ ID NO:1 that would have promoter function by describing a representative number of species of subfragments having promoter function, so that one skilled in the art would have a basis for recognizing the characteristics of SEQ ID NO:1 subfragments that retain promoter function. Here Appellants have done neither. Appellants describe only a single element that has promoter function. However, this element has only been shown to have promoter activity when linked to the rice act 2 intron 1 deletion derivative. This element appears to be a 639 base pair subfragment of the 3536 base pair sequence of SEQ ID NO:1 (examples 2 and 3 pages 112-114 of the specification, and figures 1 and 2), though it is unclear exactly which nucleotides of SEQ ID NO:1 provided this promoter function, as the specification describes the construction of the promoter containing construct only in terms of the restriction enzymes used to subclone the subfragment of SEQ ID NO:1 into the reporter construct. . . . If a nucleotide required for promoter function is not present in a given sequence, that sequence will no longer exhibit promoter function.

Unlike the specification which describes every subfragment of SEQ ID NO:1 that is between 95 and 3536 contiguous bases long, the

examiner argues that "Claim 1 encompasses every subfragment of SEQ ID NO:1 that is between 95 and 3536 contiguous bases long and that has promoter function" (EA 5; emphasis added). According to the examiner, "the description must allow those skilled in the art to recognize what regions of SEQ ID NO:1 would need to be retained in its subfragments such that the subfragments could reasonably be expected to retain promoter function" (EA 6).

As we understand the rejection, the examiner concedes that appellants' specification describes every subfragment claimed which can function as a promoter. However, that description does not satisfy the written description requirement of 35 U.S.C. § 112, first paragraph, because the subfragments of SEQ ID NO:1 between 95 and 3536 contiguous bases in length that can function as a promoter are not distinguished from the subfragments of SEQ ID NO:1 between 95 and 3536 contiguous bases in length that cannot function as a promoter. The problem with the examiner's position is that it confuses the written description requirement of 35 U.S.C. § 112, first paragraph, with the enablement requirement of 35 U.S.C. § 112, first paragraph. For example, in support of the written description requirement of 35 U.S.C. § 112, first paragraph, the examiner states (EA 5-6)(emphasis added):

> While it is not required that Appellant describe exactly the subject matter claimed, the description must allow those skilled in the art to recognize what regions of SEQ ID NO:1 would need to be retained in its subfragments such that the subfragments could reasonably be expected to retain promoter function. The Examiner maintains that the instant disclosure does not allow those skilled in the art to recognize what regions of SEQ ID NO:1 would need to be retained in its subfragments such that the subfragments could reasonably be expected to retain promoter function . . . .

The examiner's criticism that the specification would not have allowed persons skilled in the art to recognize what nucleotide subfragments of SEQ ID NO:1 function as promoters is indistinct from the concomitant criticism that the specification would not have allowed persons skilled in the art to make and use the nucleotide subfragments of SEQ ID NO:1 as promoters without undue experimentation. However, Vas-Cath, Inc. v. Mahurkar, 935 F.2d 1555, 19 USPQ2d 1111 (Fed. Cir. 1991), instructs at 1562, 19 USPQ2d at 1117:

> This court in [In re]Wilder[, 736 F.2d 1516, 1520, 222 USPQ 369, 372 (Fed. Cir. 1994), cert. denied, 469 U.S. 1209 (1985),] (and the CCPA before it) clearly recognized, and we hereby reaffirm, that 35 USC 112, first paragraph, requires a "written description of the invention" which is separate and distinct from the enablement requirement. The purpose of the "written description" requirement is broader than to merely explain how to "make and use"; the applicant must also convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention.

The invention is, for purposes of the "written description" inquiry, whatever is now claimed.

More recently, the Federal Circuit discussed both the Vas-Cath and Eli Lilly decisions (Vas-Cath, Inc. v. Mahurkar, supra; and Regents of the University of California v. Eli Lilly & Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997)), in Enzo Biochem Inc. v. Gen-Probe Inc., 296 F.3d. 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). The court stated in Enzo Biochem Inc. v. Gen-Probe Inc., 296 F.3d. at 1324, 63 USPQ2d at 1613:

> In Eli Lilly, we concluded that a claim to a microorganism containing human insulin cDNA was not adequately described by a statement that the invention included human insulin cDNA. Id. at 1557, 43 USPQ2d at 1405. The recitation of the term human insulin cDNA conveyed no distinguishing information about the identity of the claimed DNA sequence, such as its relevant structural or physical characteristics. Id. We stated that an adequate written description of genetic material "'requires a precise definition, such as by structure, formula, chemical name, or physical properties,' not a mere wish or plan for obtaining the claimed chemical invention," and that none of those descriptions appeared in that patent. Id. at 1566, 43 USPQ2d at 1404 . . . . The specification in the Eli Lilly case did not show that the inventors had possession of human insulin cDNA.

However, the court in Enzo Biochem Inc. v. Gen-Probe Inc., 296 F.3d. at 1329, 63 USPQ2d at 1616-17, clarified:

> It is true that in Vas-Cath, we stated: "The purpose of the 'written description' requirement is broader than to merely explain how to 'make and use'; the applicant must also convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she

was in possession of the invention." Vas-Cath, 935 F.2d at 1563-64, 19 USPQ2d at 1117. That portion of the opinion in Vas-Cath, however, merely states a purpose of the written description requirement, viz., to ensure that the applicant had possession of the invention as of the desired filing date. It does not state that possession alone is always sufficient to meet that requirement. Furthermore, in Lockwood v. American Airlines, Inc., we rejected Lockwood's argument that "all that is necessary to satisfy the description requirement is to show that one is "in possession" of the invention. 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997). Rather, we clarified that the written description requirement is satisfied by the patentee's disclosure of "such descriptive means as words, structures, figures, diagrams, formulas, etc., that fully set forth the claimed invention." Id.

Accordingly, we espouse the view expressed in Evans v. Eaton, 20 U.S. (7 Wheat.) 356 (1822), as did the court in Vas-Cath, Inc. v. Mahurkar, 935 F.2d at 1561, 19 USPQ2d at 1114-15, that:

> [T]he Court concluded that the specification of a patent had two objects, the first of which was "to enable artizans to make and use [the invention]. . . ." [Evans v. Eaton,] . . . at 433. The second object of the specification was
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> > to put the public in possession of what the party claims as his own invention, so as to ascertain if he claims anything that is in common use, or is already known, and to guard against prejudice or injury from the use of an invention which the party may otherwise innocently suppose not to be patented. It is, therefore, for the purpose of warning an innocent purchaser, or other person using . . . [the invention], of his infringement of the patent; and at the same time, of taking from the inventor the means of practicing upon the credulity or the fears of other persons, by

> pretending that his invention is more than what it really is, or different from its ostensible objects, that the patentee is required to distinguish his invention in his specification.

Id. at 434.

In that light, we find that here the isolated nucleic acid maize GRP promoter appellants claim comprising at least 95, 110, 125, 250, 400, 750, 1000, 1500, 2000, 2500, 3000, and 3536 contiguous nucleotide fragments of the 3536 contiguous nucleotides of SEQ ID NO:1 of Figure 4 is so precisely defined in terms of structure, formula, chemical name, and function, including Figures 1-4 and examples, that persons skilled in the art immediately would have understood what appellants claim as their invention and could readily distinguish what appellants claim from anything that is in common use, all that is known, and anything proposed for production and use in the art. If an isolated nucleotide sequence comprises at least 95 contiguous nucleotides of the 3536 contiguous nucleotides of SEQ ID NO:1 and functions as a GRP promoter when operably linked to a coding region, appellants claim it.[4] Whether the inventors "had possession of the claimed

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[4] The examiner has not adequately explained why appellant's Claims 14, 32, and 95 stand rejected under 35 U.S.C. § 112, first paragraph, for inadequate written description. As per those claims, the GRP promoter comprises the complete nucleic acid sequence of SEQ ID NO:1.

invention" (EA 3), the test the examiner used to determine compliance with the written description requirement of the first paragraph of Section 112, is not the gauge for compliance. As the court instructs in Enzo Biochem Inc. v. Gen-Probe Inc., 296 F.3d. at 1330, 63 USPQ2d at 1617:

> A showing of "possession" is ancillary to the statutory mandate that "[t]he specification shall contain a written description of the invention," and that requirement is not met if, despite a showing of possession, the specification does not adequately describe the claimed invention.

Accordingly, the examiner erred in rejecting Claims 1, 4-54, and 85-113 for noncompliance with the written description requirement of 35 U.S.C. § 112, first paragraph.

2. Rejection for nonenablement

The examiner's rejection of Claims 1, 4-54, and 85-131, all claims pending in this application, for noncompliance with the enablement requirement of 35 U.S.C. § 112, first paragraph, is an entirely distinct issue. At the onset, appellants' own specification teaches that: (1) the art is unpredictable, and (2) a considerable amount of experimentation may be required to enable persons skilled in the art to make and use the full scope of the subject matter claimed; yet the kind and amount of experimentation required to enable one skilled in the art to make

and use the full scope of the subject matter claimed is well within the knowledge and skill of a person with the ordinary level of knowledge and skill in this art to perform without undue experimentation. For example, appellants' specification teaches (Spec., pp. 12-13; emphasis added)):

> [T]he current invention includes sequences which have been derived from the maize GRP promoter disclosed herein. One efficient means for preparing such derivatives comprises introducing mutations into the sequences of the invention, for example, the sequence given in SEQ ID NO:1. Such mutants may potentially have enhanced or altered function relative to the native sequence or alternatively, may be silent with regard to function.
>
> Mutagenesis may be carried out at random and the mutagenized sequences screened for function in a trial-by-error procedure. Alternatively, particular sequences which provide the ZMGRP promoter with desirable expression characteristics could be identified and these or similar sequences introduced into other related or non-related sequences via mutation. Similarly, non-essential elements may be deleted without significantly altering the function of the elements. It further is contemplated that one could mutagenize these sequences in order to enhance their utility in expressing transgenes in a particular species, for example, maize.
>
> The means for mutagenizing a DNA segment encoding a ZMGRP promoter sequence of the current invention are well-known to those of skill in the art. Mutagenesis may be performed in accordance with any of the techniques known in the art, such as, but not limited to, synthesizing an oligonucleotide having one or more mutations within the sequence of a particular regulatory region. In particular, site-specific mutagenesis is a technique useful in the preparation of promoter mutants, through specific mutagenesis of the underlying DNA. The technique further

> provides a ready ability to prepare and test sequence variants, for example, incorporating one or more of the foregoing considerations, by introducing one or more nucleotide sequence changes into the DNA. . . . .

The specification teaches that "the technique of site-specific mutagenesis is well known in the art, as exemplified by various publications" (Spec., p. 14). "The preparation of sequence variants of the selected promoter DNA segments using site-directed mutagenesis is provided as a means of producing potentially useful species and is not meant to be limiting as there are other ways in which sequence variants of DNA sequences may be obtained" (Spec., p. 15)(emphasis added). According to the specification (Spec., pp. 15-16)(emphasis added):

> Examples of such methodologies are provided by U.S. Patent No. 4,237,224, specifically incorporated herein by reference in its entirety. A number of template dependent processes are available to amplify the target sequences of interest present in a sample, such methods being well known in the art and specifically disclosed herein below.
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> One efficient, targeted means for preparing mutagenized promoters or enhancers relies upon the identification of putative regulatory elements within the target sequence. This can be initiated by comparison with, for example, promoter sequences known to be expressed in a similar manner. Sequences which are shared among elements with similar functions or expression patterns are likely candidates for the binding of transcription factors and are thus likely elements which confer expression patterns. Confirmation of these putative regulatory elements can be achieved by deletion analysis of each putative regulatory region followed by function analysis of each deletion construct

by assay of a reporter gene which is functionally attached to each construct. As such, once a starting promoter or intron sequence is provided, any of a number of different functional deletion mutants of the starting sequence could be readily prepared.

As indicated above, deletion mutants of the ZMGRP promoter also could be randomly prepared and then assayed. With this strategy, a series of constructs are prepared, each containing a different portion of the clone (a subclone), and these constructs are then screened for activity. A suitable means for screening for activity is to attach a deleted promoter construct to a selectable or screenable marker, and to isolate only those cells expressing the marker protein. In this way, a number of different, deleted promoter constructs are identified which still retain the desired, or even enhanced, activity. The smallest segment which is required for activity is thereby identified through comparison of the selected constructs. This segment may then be used for the construction of vectors for the expression of exogenous protein.

The specification also generally describes various regulatory elements (Spec., pp. 18-21), terminators (Spec., p. 21), transit or signal peptides (Spec., pp. 21-23), marker genes (Spec., pp. 23-27), and exogenous genes for herbicide resistance, insect resistance, environment or stress resistance, disease resistance, mycotoxin reduction, grain quality, etc. (Spec., pp. 27-61), which are suitable for use in modifying plant characteristics, and include citations to prior art and summaries of the state of the art. The specification thereafter discusses assays which may be employed to determine levels of expression of new transgenic DNA

constructs (Spec., pp. 61-108) and various art recognized methods suitable for plant transformation, growth, stabilization, regeneration, seed production, and breeding (Spec., pp. 69-74), including liberal citation of the prior art and discussion of the state of the art. Following the aforementioned teachings, the specification introduces the examples presented as follows (Spec., pp. 110-111)(emphasis added):

> The following examples are included to demonstrate preferred embodiments of the invention. It should be appreciated by those of skill in the art that the techniques disclosed in the examples which follow represent techniques discovered by the inventor to function well in the practice of the invention, and thus can be considered to constitute preferred modes for its practice. However, those of skill in the art should, in light of the present disclosure, appreciate that many changes can be made in the specific embodiments which are disclosed and still obtain a like or similar result without departing from the concept, spirit and scope of the invention. . . . .
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> . . . . .
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> The current inventors have demonstrated the utility of a novel maize promoter, designated Zea Mays Glycine Rich Protein (ZMGRP) promoter, in conjunction with an intron in transgenic maize. The ZMGRP promoter comes from a gene (Genbank Acc# GI/22312) that is induced in response to water stress and wounding. The ZMGRP mRNA has been shown to accumulate in epidermal cells upon induction (Gomez et al., 1988). The ZMGRP promoter was isolated from a maize B73 genomic library and fused to the gus reporter gene, both with and without a modified intron from the rice Act2 gene (see Example 5).

> Transient expression assays in microparticle bombarded maize suspension cells and in excised maize root and leaf tissue were carried out in order to determine the activity of the ZMGRP promoter. The promoter was shown to be functionally active in conjunction with a modified actin 2 (Act2) intron 1. Furthermore, the ZMGRP promoter - Act2 intron combination yielded transient expression levels that were at least 70% the level observed from the rice actin 1 (Act1) promoter - intron combination (Zhang, W., McElroy, D., Wu, R., 1991). Finally, the ZMGRP promoter - intron - gus construct was shown to express high levels of GUS protein in the leaves, stems and meristematic regions of the roots of R_0 maize plants regenerated from transformed maize callus.

Accordingly, appellants argue that the broad teachings of the specification and claims are supported by a number of specific examples of isolated DNA comprising at least 95 contiguous bases of SEQ ID NO:1 which comprise a functional maize GRP promoter. We examine those examples below.

Example 1 teaches that the inventors serendipitously isolated the ZMGRP promoter "from a maize B73 size-selected lambda genomic DNA (gDNA) library while attempting to isolate a second maize promoter, designated A3" (Spec., p. 111). Example 1 reports (Spec., p. 112):

> The analysis revealed that the restriction map and hybridization pattern of the putative clone was highly similar to, but not identical to, the expected A3 pattern. Partial sequencing of the clone revealed that the 5' sequence was highly homologous, but not identical to that of the A3 5' region. A GenBank search revealed that the 4000 base pair cloned sequence shared homology in

about the 400 most 3' based pairs with an ABA-inducible genomic clone reported by Gomez et al. (1988)(GenBank Accession Number X12564).

Example 2 characterizes the ZMGRP promoter constructs used in subsequent examples of transient expression analyses and transformations therewith. Example 2 in its entirety reads (Spec., pp. 112-113)(emphasis added):

> Sequence characterization of the ZMGRP promoter-containing plasmid revealed that the ~ 4.0 kb SacI insert contained a HindIII site 97 bp from the 5' end of the insert and approximately 360 bp of ZMGRP coding sequence 3' of the ATG start codon. Restriction enzyme analysis determined that there was a unique XhoI site approximately 400bp 5' of the ATG start site. The sequence around the XhoI site was determined and used to design a 5' PCR primer. A 3' PCR primer was designed to change the sequence around the ATG start site to create an NcoI site and to introduce a SmaI site 4 bp 5' of the ATG start codon. These primers were used to PCR amplify the DNA at the 3' end of the promoter from the XhoI site to the newly created NcoI site. The PCR fragment was used in a three way ligation, employing a HindIII to XhoI fragment containing the 5' ~3.2kbp part of the ZMGRP promoter region, the XhoI to NcoI fragment containing the 3' 0.4 kbp part of the ZMGRP promoter region, and the gus-nos sequence containing vector pGN73, which had been digested with HindIII and NcoI. The resulting construct was designated pZMGRP-GN73 (Fig. 2, SEQ ID NO:2)[5]. A construct designated pZMGRP-Act2-int-GN73 was made by replacing the SmaI - NcoI region of the ZMGRP promoter with a PvuII - NcoI restriction fragment from pDPG836 containing a rice Act2 intron 1 deletion derivative (Act2-int)(Fig. 1, SEQ ID NO:3)[6].

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[5] SEQ ID NO:2 includes 8076 nucleotides (Raw Sequence Listing (Paper No. 4)).

[6] SEQ ID NO:3 includes 9002 nucleotides (Raw Sequence Listing (Paper No. 4)).

Example 3 (Transient Expression Analysis of ZMGRP Promoter Expression Function) describes the transient expression assays used for analysis of (Spec., p. 113):

> . . . expression of the gus reporter gene (E. coli beta-glucuronidase) fused to the ZMGRP promoter with an actin 2 intron (U.S. Serial No. 09/312,304) (ZMGRP (639) act 2 pGN73, FIG. 1) or without any intron (ZMGRP (639) pGN73, FIG. 2) . . . .

Having considered the teaching in appellants' specification, we now focus on the examiner's reasons to doubt the objective truth of the statements contained therein. In re Marzocchi, 439 F.2d 220, 223-24, 169 USPQ 367, 369-70 (CCPA 1971), instructs (footnote omitted):

> As a matter of Patent Office practice . . . a specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as in compliance with the enabling requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support. . . . .
>
> . . . Most often, additional factors, such as the teachings in pertinent references, will be available to substantiate any doubts that the asserted scope of objective enablement is in fact commensurate with the scope of protection sought and to support any demands based thereon for proof. . . . [I]t is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or

reasoning which is inconsistent with the contested statement.

To satisfy the enablement requirement of 35 U.S.C. § 112, first paragraph, for the full scope of contiguous nucleotide sequences appellants claim,

> . . . the specification [must] . . . enable any person skilled in the art to which it pertains to make and use the claimed invention. Although the statute does not say so, enablement requires that the specification teach those in the art to make and use the invention without "undue experimentation." In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). That some experimentation may be required is not fatal; the issue is whether the amount of experimentation required is "undue." Id. at736-37, 8 USPQ2d at 1404.

In re Vaeck, 947 F.2d 488, 495, 20 USPQ2d 1438, 1444 (Fed. Cir. 1991). As explained in In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404 (footnotes omitted), "Enablement is not precluded by the necessity for some experimentation such as routine screening." In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404, amplified the statement with a quote from Ex parte Jackson, 217 USPQ2d 804, 807 (Bd. App. 1982)(emphasis added):

> The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed.

In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404, instructs (footnote omitted):

> Factors to be considered in determining whether a [redacted] disclosure would require undue experimentation have been summarized by the board in Ex parte Forman[, 230 USPQ 546, 547 (Bd. Pat. App. & Int. 1986)]. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

There appears to be minimal differences in appellants' and the examiner's respective views of the evidence relative to each of the factors material to their respective determinations whether or not appellants' specification would have required persons skilled in the art to make and use the full scope of the claimed invention without undue experimentation. On balancing the weight of the collective evidence relating to all the material factors, the scales do not significantly sway one way or another. Appellants and the examiner appear to agree that, for any person skilled in the art to make and use the full scope of the claimed invention, a considerable amount of trial and error experimentation would be required. However, the specification provides a considerable amount of direction and guidance in that effort and cites prior art which suggests that the kind and amount of experimentation are routine. Appellants point to their working examples, but the examiner finds the whole and only one functionally effective 639 bp

fragment of the whole 3536 bp nucleotide appellants describe, and [illegible] the 639 bp fragment is defined solely in terms of its enzymatic restriction sites. The number of promoters which have been used to effect expression of phenotypic genetic codes appears to be small, yet appellants serendipitously have discovered one which preferably promotes expression of a gene to which it is fused only when a plant transformed by the construct is stressed and disclosed its sequence and functional properties in the application before us. The claims are narrowly limited to promoters having 3536 contiguous named nucleotides and functionally effective fragments thereof having at least 95 contiguous nucleotides. The prior art cited by the examiner relating to the activity and requisite functional sequences of the cauliflower mosaic virus 35S and nopaline synthase (nos) promoters does show that the nucleotide structure essential for promoter activity is highly unpredictable. However, the same prior art shows that the level of skill and knowledge in this art is extremely high, that mutations and deletions to the basic sequence more often than not lower rather than eliminate promoter activity, and that it is well within the ordinary skill of the artisan to determine those nucleotide sequences which are critical for functional activity.

Having considered all the evidence, we are not convinced that the examiner has satisfied her burden to show that, in light of the guidance and direction provided by appellants' specification, the kind and amount of experimentation required of one skilled in the art to make and use the full scope of the subject matter claimed is more than routine.

More significantly, however, the examiner urges (EA 8-9) (emphasis added):

> Appellants need to provide sufficient guidance for one skilled in the art to determine which of the claimed subfragments of SEQ ID NO:1 would be likely to have promoter function. In the absence of such guidance, it would require undue experimentation for one skill[ed] in the art to practice the claimed invention, because the ability of a particular nucleic acid sequence to function as a promoter is highly unpredictable on the basis of nucleotide sequence information alone. . . . . The examiner maintains that to provide sufficient guidance for one skilled in the art to determine which sequences have promoter function, the specification must provide some indication of what specific nucleotides the sequences must retain in order to retain promoter function. Appellants need not describe why or how the invention works in order to provide such guidance.

Also see the examiner's rationale below (EA 11):

> The examiner does not assert that one skilled in the art would be without sufficient guidance in obtaining the claimed contiguous subfragments because the specification does not provide sufficient structural and functional information to prepare the recited sequences. The examiner asserts that one skilled in the art would be without sufficient guidance in recognizing the claimed contiguous subfragments that

> have promoter activity because the specification does not provide sufficient structural and functional information for one skilled in the art to recognize which sequence has promoter function.

In the two quotations reproduced above, we find the origins of the examiner's reversible error in this case.

Even in an unpredictable art, this being one, it is legal error for an examiner to require an applicant to disclose a common chemical structure essential for functional activity, here the nucleotide sequence of the maize GRP promoter of SEQ ID NO:1 critical for functional activity, to satisfy the enablement requirement of 35 U.S.C. § 112, first paragraph. To enable persons skilled in the art to make and use the full scope of the subject matter claimed, here all the subfragments of SEQ ID NO:1 which are in fact active as maize GRP promoters, (1) it may not be necessary to disclose, or even know, the chemical structure essential for functional activity in order to enable any person skilled in the art to make and use the full scope of the subject matter claimed, and (2) there may not be a common chemical structure essential for functional activity of the full scope of the subject matter claimed. While each case must be considered on its own facts, we are directed to reverse the examiner's rejection of appellants' claims under 35 U.S.C. § 112, first paragraph, as explained in the

examiner's answer, by In re Angstadt, 537 F.2d 498, 503-04, 190 USPQ 214, 218-219 (CCPA 1976):

> If . . . the disclosure must provide "guidance which will enable one skilled in the art to determine, with reasonable certainty before performing the reaction, whether the claimed product will be obtained" (emphasis in original), as the dissent claims, then all "experimentation" is "undue," since the term "experimentation" implies that the success of the particular activity is uncertain. Such a proposition is contrary to the basic policy of the Patent Act, which is to encourage disclosure of inventions and thereby to promote progress in the useful arts. To require disclosures in patent applications to transcend the level of knowledge of those skilled in the art would stifle the disclosure of inventions in fields man understands imperfectly, like catalytic chemistry. The Supreme Court said it aptly in Minerals Separation, Ltd. v. Hyde, 242 U.S. 261, 270-271 (1916) . . . :
>
> > . . . the certainty which the law requires in patents is not greater than is reasonable, having regard to their subject matter . . . .
>
> Appellants have broadly disclosed a class of catalyst complexes whose use they deem to be part of the invention. But for this disclosure the public may have been deprived of the knowledge . . . . In this art, the performance of trial runs using different catalysts is "reasonable," even if the end result is uncertain . . . .

We have considered the examiner's explanations, appellants' responses, and all the evidence for and against the patentability of appellants' claims under 35 U.S.C. § 112, first paragraph, in light of the guidance our reviewing courts have provided.

Accordingly, we reverse the examiner's final rejections of Claims 1, 4-54, and 85-131 for noncompliance with description and enablement requirements of 35 U.S.C. § 112, first paragraph.

Conclusion

For the reasons stated herein above, it is

ORDERED that the examiner's rejections of Claims 1, 4-54, and 85-113 for noncompliance with the written description requirement of 35 U.S.C. § 112, first paragraph, is REVERSED; and

FURTHER ORDERED that the examiner's rejections of Claims 1, 4-54, and 85-131 for noncompliance with the enablement requirement of 35 U.S.C. § 112, first paragraph, is REVERSED.

REVERSED

SHERMAN D. WINTERS)
Administrative Patent Judge)
)
)
)
TEDDY S. GRON) BOARD OF PATENT
Administrative Patent Judge) APPEALS
) AND
) INTERFERENCES
)
)
)
LORA M. GREEN)
Administrative Patent Judge)

Appeal No. 2003-0936
Application No. 09/532,806

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